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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/255,963	02/23/99	MA	P UM-03646

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EXAMINER	
STROUP,C	
ART UNIT	**PAPER NUMBER**
1633	8

DATE MAILED: 09/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/255,963	Ma, P.X.
Examiner	**Group Art Unit**
Stroup, Carrie	1633

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-38 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-38 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4,6

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Applicant's preliminary amendment Paper 7, filed August 31, 2000, has been entered. Claims 1-20 have been amended. Claims 21-38 have been added. Claims 1-38 are currently pending in the present application.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

2. Claims 1, 3-7, 9, 23-28, and 33-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Draget et al (1991).

Applicant's claimed invention is to a product, and a method of making in vitro, consisting essentially of a sodium alginate salt, or alginate derived from *Marocystis pyrifera* or *Laminaria hyperbores* , calcium carbonate, and D-glucono-δ-lactone (also known as GDL), wherein the ratio of calcium carbonate to GDL is .5, and the thickness is between 4-8mm and the diameter approximately 18mm.

Draget et al teach the formation of a gel consisting of mixing 15mM $CaCO_3$ with sodium alginate solution, then adding 30mM GDL, resulting in a final gel of pH 7 (see, e.g., pg 161, para. 2). Draget et al also teach that the sodium alginate can be substituted with alginate derived from *Marocystis pyrifera* or *Laminaria hyperbores*, thus

altering the viscosity of the gel (pg 161, Table 1; pg 173); and that the dimensions of the gel (e.g. thickness and diameter) are largely a function of the dimensions of the mold into which they form, and can thus be easily modified by one of ordinary skill in the art. Therefore, the claimed invention was clearly anticipated.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 2, 8, 10, 11-22, 29-32 , 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Draget et al (1991) as applied to claims 1, 3-7, 9, 23-28, and 33-36 above, and further in view of Hauselmann et al (US Patent 5,658,343) and Cao et al (1996).

Applicant's claimed invention is to a product, a method of making in vitro, and a method of use in tissue engineering comprising a product consisting essentially of a sodium alginate salt, or alginate derived from *Marocystis pyrifera* or *Laminaria hyperbores* , calcium carbonate, and D-glucono-δ-lactone (also known as GDL), wherein the ratio of calcium carbonate to GDL is .5; the thickness is between 4-8mm and the diameter approximately 18mm; the calcium ion to carboxyl molar ratio is .27, .09 to .9, or .18 to .72; and the swelling of the hydrogel as a function of the calcium ion concentration. The method may also comprise the addition of cells in vitro, such as osteoblasts, and for the implantation of the product.

Draget et al teach the formation of a gel consisting of mixing 15mM $CaCO_3$ with sodium alginate solution, then adding 30mM GDL, resulting in a final gel of pH 7 (see, e.g., pg 161, para. 2). Draget et al also teach that the sodium alginate can be substituted with alginate derived from *Marocystis pyrifera* or *Laminaria hyperbores,* thus altering the viscosity of the gel (pg 161, Table 1; pg 173); and that the dimensions of the gel (e.g. thickness and diameter) are largely a function of the dimensions of the mold into which they form, and can thus be easily modified by one of ordinary skill in the art. Draget et al does not teach the use of cells in said method, a method of tissue engineering, the implantation of the gel, or the ratio of calcium ions to carboxyl groups.

Hauselmann et al teach the method of producing an alginate gel in vitro comprising cells that produce an extracellular matrix, for implantation in vivo (e.g., col. 1, lines 39-60). Hauselmann et al also teach that the molar ratio of calcium ions to carboxyl groups in the gel determines the amount of crosslinking of the gel, as well as the amount of swelling and thus size of the gel (e.g, col 7, lines 29-46, & Figure 6a,b).

Cao et al teach the method of making and using biodegradable calcium alginate gels with osteoblasts in vitro for implantation in vivo to generate bone growth (abstract).

Therefore, in light of Draget, Hauselmann, and Cao et al it would have been obvious to one of ordinary skill in the art to add cells, such as osteoblasts, to the composition disclosed by Draget. One would have been motivated to do this to utilize the gel as a scaffold for cell growth and differentiation, otherwise known as tissue engineering, both in vitro for implantation, or for injection and solidification in vivo, such as taught by Hauselmann and Cao. One would also have been motivated to alter the calcium ion concentration and the ratio of calcium ions to alginate carboxyl groups in order to alter the amount of H2O binding to the matrix, and hence the amount of gel swelling and size of the gel, because Hauselmann et al disclose that this procedure is widely known and used in the art of hydrogels (e.g, Figure 6a,b). Therefore, the claimed invention of claims 10, 21, 22, 29-32, 37, and 38 pertaining to specific ion

concentrations and molar ratios resulting in hydrogel swelling and shrinking are result effective variables which could readily been determined by one of ordinary skill in the art.

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carrie Stroup whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached at (703) 308-0447. The fax phone number for this Group is (703) 308-8724.

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